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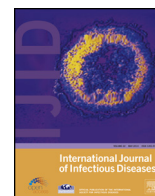
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Medical Imagery

Two cases of erythema induratum of Bazin – a rare cutaneous manifestation of tuberculosis



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SUMMARY

Tuberculosis remains a global disease burden, counting more than 9 million new cases per year. Tuberculosis is caused by infection with *Mycobacterium tuberculosis*-complex. Though most commonly affecting the lungs, any organ can become a site of tuberculous infection. Cutaneous tuberculosis is rare, representing 1–2% of all cases of tuberculosis. There are numerous different cutaneous manifestations of tuberculosis. We describe two cases of erythema induratum of Bazin, a so-called tuberculid manifestation of cutaneous TB. Both cases are patients from endemic areas. In the cases presented, there were no signs of other organs affected, and cutaneous lesions disappeared during anti-tuberculous treatment.

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1. Introduction

Since the late 80s, industrialized countries have experienced an increasing incidence of tuberculosis (TB), mainly due to immigration. This has led to new health challenges. Even though the notification rates of overall TB and pulmonary TB have been decreasing in the European Union/European Economic Area since 2002, the proportion of extrapulmonary TB has increased from 16.4% in 2002 to 22.4% in 2011.¹

Cutaneous manifestations of TB are rare, and represents 1–2% of all TB-cases.² We describe two cases of erythema induratum of Bazin (EIB), a rare cutaneous manifestation of TB, in immigrants from endemic areas, presented with no or few symptoms of active TB.

2. Case presentation

2.1. Case #1

An Afghan male, age 45, was referred for dermatological evaluation due to round, tender, erythematous skin lesions on both lower extremities, sized 1–3 cm in diameter. The patient had fled from Afghanistan over Pakistan to Denmark one year prior to initial evaluation. He was reported previously healthy and without any medication. The skin lesions had been present for some months. The patient reported no night sweats, no weight loss and no pulmonary symptoms.

A punch skin biopsy was performed, and standard histology showed lobar panniculitis with focal non-caseous necrosis,

vasculitis and granulomas (Figure 1A–D). No acid-fast bacilli were demonstrated. The patient was found to have a strong positive Interferon Gamma Release Assay (IGRA)-reaction (Quantiferon®-TB Gold, Cellestis, Ltd., Carnegie, Australia) for *M. tuberculosis* infection. Chest x-ray was normal, and the patient's blood samples were without suspicious findings. The patient was tested negative for HIV and chronic viral hepatitis B and C. Due to the absence of pulmonary symptoms, the positive IGRA was interpreted as a manifestation of latent TB, and the patient underwent six months of mono-therapy with isoniazid and pyridoxine. The skin eruptions were still present at the end of treatment.

The patient was re-evaluated one year after end of treatment. He had increasing dyspnoea, but no expectoration. He had persistent and new onset of skin eruptions, and a repeated skin biopsy showed lobar panniculitis. The IGRA was still positive, and the skin biopsy was polymerase chain reaction (PCR)-negative for *M. tuberculosis*-complex. A positron-emission-tomography-CT (PET-CT) scan revealed one FDG-positive lymph node in the right lung. Biopsy from this lymph node showed numerous lymphocytes, but no acid-fast bacilli or malignant cells. PCR was negative for *M. tuberculosis*-complex. Due to positive IGRA and the histological changes found in the punch skin biopsy, skin lesions were interpreted as erythema induratum of Bazin (EIB). The patient underwent 8 weeks of treatment with ethambutol, rifampicin, moxifloxacin and pyrazinamide, followed by 16 weeks of rifampicin and moxifloxacin. The skin eruptions gradually shrunk, and had disappeared before end of treatment. Prior to initiation of treatment, the patient was evaluated for sarcoidosis and asthma by

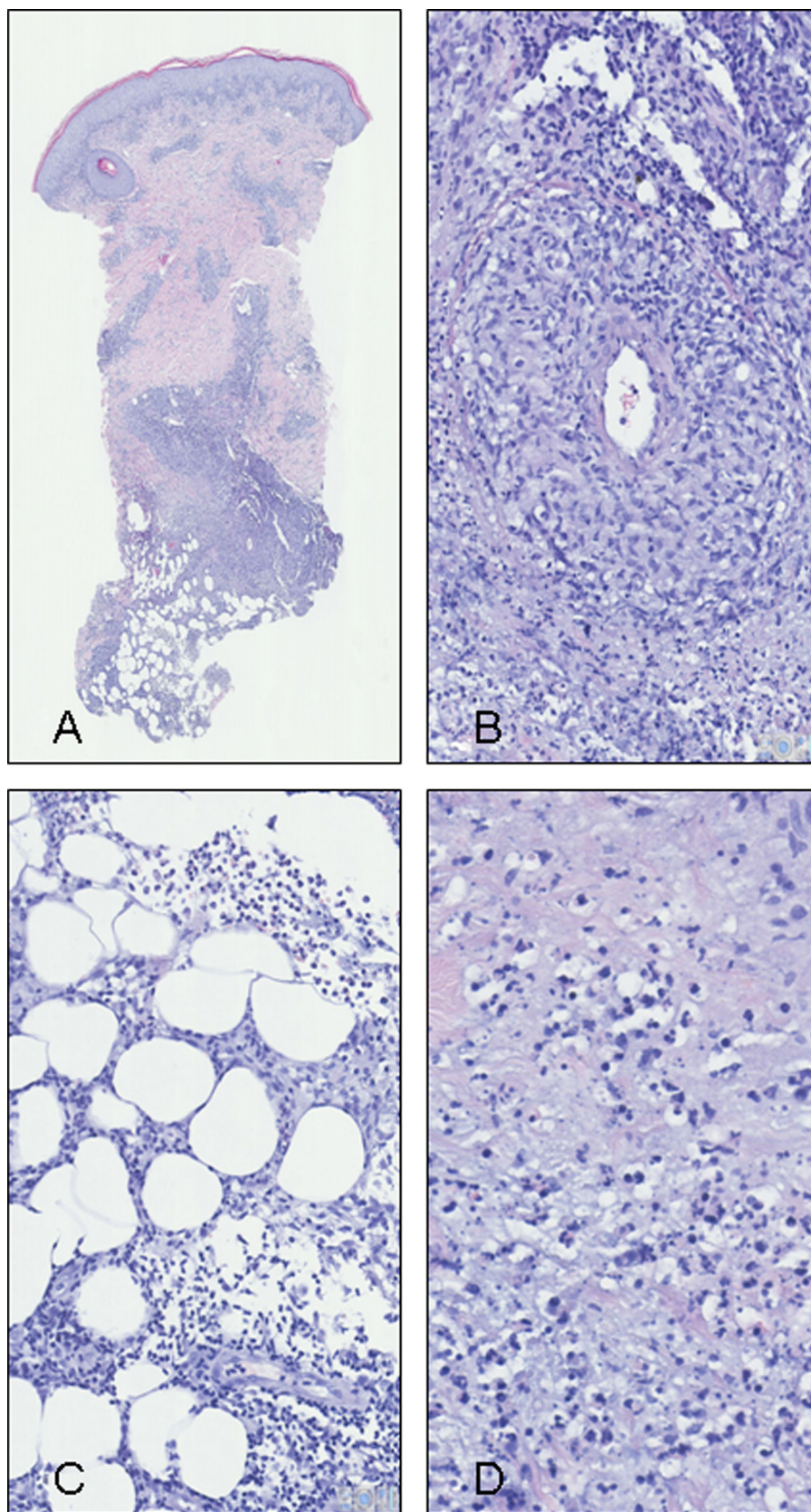


Figure 1. Histopathological findings of erythema induratum of Bazin.

A, Punch biopsy of the skin. B, There is vasculitis, focally granulomatous. C, Deep dermal and subcutaneous inflammation with a dense diffuse neutrophilic and granulomatous infiltrate. D, Widespread leukocytoclasia and necrosis without caseation. (hematoxylin-eosin, original magnifications x 30 (A), x 300 (B and C) and x 500 (D)).

a consultant in pulmonary medicine, but neither was confirmed. The dyspnoea disappeared during treatment.

2.2. Case #2

A 67-year old woman from Romania was referred to dermatological evaluation for tender, round skin-eruptions, primary located on the trunk and lower extremities. The patient had been living in Denmark for the last 30 years, and had no known exposure to TB.

The skin eruptions had been present on/off for the last 25 years, with spontaneous regression some months after presence. Punch skin biopsy revealed non-caseous necrotising panniculitis, with no demonstrated acid-fast bacilli. PCR-assay of the skin biopsy was negative for *M. tuberculosis*-complex. The patient had a strong positive IGRA-reaction. Other blood samples were within reference intervals, and a chest x-ray was normal. The patient was tested negative for HIV and chronic viral hepatitis B and C. The clinical and histologic picture was consistent with EIB.

The patient underwent anti-tuberculous treatment, and the skin lesions shrunk in size. After six months of treatment, a few smaller and painless lesions were still present, and treatment was continued for another three months with acceptable response.

3. Discussion

Cutaneous TB is classified into multibacillary and paucibacillary forms.² Multibacillary forms demonstrate acid-fast bacilli in biopsies, and include tuberculous chancres, scrofuloderma and perforating TB. Paucibacillary forms include TB- verrucosa cutis, lupus vulgaris and tuberculids, and are characterized by the possible absence of acid-fast bacilli. Tuberculids include papulonectrotic tuberculid, lichen scrofulosorum and erythema induratum of Bazin (EIB). Although rare in Western countries, EIB is the most common of the tuberculids. EIB shows female predominance, and the cutaneous lesions often occur on the lower extremities. The lesions are described as tender, erythematous and may vary from 1 to 5 cm in size. The skin lesions may ulcerate, and can in these cases cause permanent scarring and/or hyperpigmentation (Figure 2 – please note that the photo provided is not from the cases described above, but lesions from the cases were similar).

EIB is caused by infection with *M. tuberculosis*-complex. The direct cause of the skin lesions is unknown, but is thought to be caused by autoimmune reaction to the presence of the acid-fast bacilli. EIB shows similarities to nodular vasculitis, which can be caused by sarcoidosis, chronic hepatitis C and other chronic inflammatory conditions. Both conditions represent a hypersensitivity reaction to antigens, e.g. tubercle bacilli. Positive IGRA can support infection with *M. tuberculosis*-complex, and is thus useful in differentiation between EIB and other causes of nodular vasculitis.³

Case 1 was re-evaluated due to increasing dyspnoea after six months of mono-therapy with isoniazid. Since he showed no expectoration, weight loss or night sweats, and no signs of infiltration by PET-CT, pulmonary TB was not suspected. Since EIB is regarded as an autoimmune reaction, a possible explanation for the dyspnoea is a component of pulmonary vasculitis.

Histologic findings of EIB are non-specific, and include mixed septal and lobular panniculitis with varying combinations of vasculitis, septal fibrosis, granulomatous inflammation and necrosis, which may be caseation-like (Figure 1A-D).⁴



Figure 2. Macroscopic skin changes that are found in erythema induratum of Bazin. Tender, round, erythematous (approx. 3 cm in size) lesion localized to the calf. Please note that the photo provided is not from the cases described above, but lesions from the cases were similar.

Photo courtesy to professor Niels K. Veien, Danderm.

Treatment of EIB does not differ from conventional antituberculous therapy. In the first case described here, moxifloxacin was included, since the patient previously underwent six months of isoniazid therapy for suspected latent TB, resulting in possible isoniazid resistance. Skin lesions may be treated with potassium iodide, but evidence of efficacy is sparse.⁵

We have described two cases of EIB in patients with no obvious symptoms of active TB, who were born in TB-endemic countries, where IGRA has limited clinical relevance in active TB. Still IGRA was in these cases useful in strengthening a clinical suspicion of EIB. However, the confirmation of the diagnosis lay somewhat in the favourable treatment outcome in both cases.

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